

## **REMARKS**

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments and remarks herein, which place the application in condition for allowance.

### **I. STATUS OF CLAIMS AND FORMAL MATTERS**

Claims 1-23 are pending in this application. Claims 17, 19 and 20 have been amended for clarification. Support for the amended claims can be found throughout the specification and claims as originally filed. Claim 3 has been cancelled solely to expedite prosecution. Claim 4 has been amended to correct dependency. Claims 6 and 8 have been amended to correct typographical errors. No new matter has been introduced.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. It is submitted that the amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, these amendments are made simply for clarification.

The issues raised by the Examiner in the Office Action are addressed below in the order they appear in the prior Action.

### **II. PRIORITY OF THE APPLICATION**

The Examiner contends that the instant application is not entitled to the benefit of priority of the application filed December 19, 2003, asserting that it does not provide support for “each concentration range of the recited ingredients, as well as the pH range recited in claim 13” of the subject application filed March 1, 2004. Applicants traverse the Examiner’s contention that the priority date of the instant claims is the filing date of the current application, March 1, 2004.

The subject application claims the benefit of priority of U.S. Provisional Application No. 60/530,939 (the ‘939 application), filed December 19, 2003.

The Examiner’s attention is drawn to *In re Davies*, 177 USPQ 381 (CCPA 1973). In *Davies*, the applicants were seeking to rely upon unexpected properties that may not have been disclosed in their application. At page 385 the *Davies* Court states (with emphasis added):

But, if the applicant can be required to include the property in his specification without prejudice to him, a compromise is reached upon which the evidentiary ruling can be based.

**We think such a compromise is possible as we see no impediment to the present appellants' re-filing their application and incorporating a discussion of the allegedly unobvious properties while retaining the effective filing date of the application involved here through § 120. ... We certainly do not think the newly disclosed properties alter the subject matter sought to be patented.**

The '939 application discloses the invention that "provides for the method to extend the shelf life of an active ingredient in a drug comprising increasing the amount of an already existing antioxidant or stabilizer in the formulation of said drug to decrease or to prevent the formation of acid/base catalyzed decomposition of said active ingredient" (page 4), which is identical to the method presently claimed. Both applications disclose stabilized feed premix formulations comprising at least one avermectin or milbemycin as an active ingredient and anhydrous citric acid as a stabilizer. The '939 application discloses exactly the same components of the claimed formulation recited in the pending claims. All the concentration ranges of the ingredients recited in the claims of the '939 application are fully incorporated in the pending claims. Although the pH range is not specifically recited in the '939 application, it is clear that the earlier claimed stabilized feed premix formulations were prepared under the same pH as both applications have identical preparation procedures (Example 1 in both applications) and stability results for the claimed formulations (Table I in the '939 application and Table II in the present application).

Thus, contrary to the Examiner's assertion, the subject application is entitled to the priority date of December 19, 2003, the filing date of the '939 application.

### **III. THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, ARE OVERCOME**

Claims 3, 17 and 19 are rejected under 35 U.S.C. § 112, second paragraph as allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner contends that the recitation “insect growth-regulating compound is one that mimics juvenile hormones” in claim 3 cannot be precisely determined. The Examiner also alleges that the recitation “increasing the amount of the already existing stabilizer” in claim 17 lacks clarity. The Examiner further asserts that it is unclear whether the amount of stabilizer in claim 19 refers to the original amount or the amount added to decrease the pH of the premix.

Claim 3 has been cancelled solely to expedite prosecution, thereby rendering the rejection of this claim moot.

Claim 17 has been amended to clarify that an additional amount of stabilizer compared to the amount of stabilizer used in the original formulation is used in extending the shelf life of a premix formulation.

Claims 19 and 20 have been amended to clarify that the amount of stabilizer is the additional amount.

In view of the foregoing amendments, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, are respectfully requested.

#### **IV. THE DOUBLE PATENTING REJECTION IS OVERCOME**

Claims 1-16 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3, 7 and 9-19 of copending Application No. 11/107,048 in view of U.S. Patent Nos. 4,199,569 and 4,910,219.

According to PAIR, claims 1-32 of copending Application No. 11/107,048 have been cancelled, thereby rendered the rejection moot. Accordingly, reconsideration and withdrawal of the nonstatutory obviousness-type double patenting rejection are respectfully requested.

#### **V. THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ARE OVERCOME**

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse.

The test for enablement requires a determination of whether any person skilled in the art can make and use the invention without undue experimentation. *See In re Wands*, 858 F.2d 731, 8 U.S.P.Q.2d 1400, (Fed. Cir. 1988). The factors involved in determining whether there is sufficient evidence to support a finding of enablement include, among others, (1) the breadth of

the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *See Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404.

Applicants respectfully assert that when read in view of the specification, the pending claims are enabled.

The Examiner states that “formulations comprising avermectins and milbemycins are known to be unstable and to undergo substantial decomposition due to heat and moisture sensitivity” according to Maxfield et al. (U.S. Patent No. 4,597,969), thus alleging that shelf life of the claimed formulations is unpredictable and difficult to maintain.

The reference cited by the Examiner relates to a method of granulation for the stabilization of unstable or heat-sensitive animal drugs or food supplements comprising avermectins and milbemycins. The current invention teaches the extension of shelf life by decreasing or preventing acid or base catalyzed decomposition of avermectin and milbemycin derivatives by controlling the amount of stabilizer in the premix formulation in an amount effective to adjust the pH range to between about 4 to about 6. Both the subject invention and Maxfield recognize that formulations comprising avermectins and milbemycins can be unstable and can undergo substantial decomposition. However, contrary to the Examiner’s assertion, the subject application provides methods for successful stabilization and extension of shelf life of the claimed formulations.

The Examiner alleges that “the disclosure is clearly not predictable for formulations comprising milbemycins, optionally with an insect growth-regulating compound, or a stabilizer other than anhydrous citric acid”. A person skilled in the art can easily derive from the instant specification that the present invention can be applied to milbemycins and that other stabilizers can be used to decrease or to prevent the acid/base catalyzed decomposition of the active ingredient in the claimed formulation. Decomposition of milbemycins can be related to base catalyzed decomposition (Figure 1), which leads to epimerization at C2 and isomerization of the double bond between C3 and C4. Milbemycins lack saccharide substituents, so they are not subjected to acid catalyzed decomposition. Maintaining pH between 4 and 6 in formulations containing milbemycins would decrease or prevent decomposition as well as in formulations

containing avermectins, since decomposition of milbemycins is more likely to happen at a more basic pH. For milbemycins, anhydrous citric acid as well as other stabilizers recited in the instant specification (paragraph 0038) can be used to adjust the pH range to between 4 and 6.

The Examiner asserts that the pending claims are “extremely broad and inclusive of any anthelmintics avermectin or milbemycin, formulated with numerous pharmaceutically acceptable surfactants, waxes, antioxidants, carrier vehicles, stabilizers and, optionally, at least one insect growth-regulating compound”. The pending claims recite premix formulations and a method for increasing the shelf life of formulations comprising avermectin or milbemycin compounds. The breadth of the claims is not unduly broad as the method of extending the shelf life of premix formulations relates to compositions comprising avermectin or milbemycin derivatives susceptible to acid/base catalyzed decomposition.

The Examiner also asserts that no results for other premix formulations wherein a milbemycin or a different stabilizer is employed are provided. Table II presents results that are intended to illustrate the general affect of the additional amount of stabilizer on stability of the disclosed formulations. The use of ivermectin and citric acid are only illustrative of one embodiment. Stability of the claimed formulations depends on maintaining the pH between 4 and 6 to decrease or prevent acid/base catalyzed decomposition of the active ingredients. The improved stability can be achieved with any of the claimed stabilizers that are capable of maintaining the desired pH range in the claimed formulations comprising avermectins or milbemycins that undergo acid or base catalyzed decomposition.

In view of the statements above, the breadth of the claims is not unduly broad, the amount of direction provided by the instant specification is high particularly in regard to the inclusion of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure is therefore low and, in any event, would not constitute undue experimentation.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, first paragraph, are respectfully requested.

## **VI. THE REJECTIONS UNDER 35 U.S.C. § 103(a) ARE OVERCOME**

Claims 1-23 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Beuvry et al., U.S. Patent No. 5,824,653, in view of Katoh et al., U.S. Patent No. 4,939,166,

Chabala et al., U.S. Patent No. 4,199,569, Sutherland et al., U.S. Patent No. 4,910,219, Freehauf et al., U.S. Patent No. 7,001,889, and Carson et al., U.S. Patent No. 6,548,478. Applicants respectfully traverse.

Establishing a *prima facie* case of obviousness requires that the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP 2143.

The Examiner is respectfully reminded of the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). As stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): “The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the prior art suggests the desirability of the modification.” Furthermore, the Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: “[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.” *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_\_ (2007).

Applying the law to the instant facts, the references relied upon by the Office Action do not disclose, suggest or enable Applicants’ invention.

The Examiner states that Beuvry teaches anthelmintic compositions comprising avermectins, milbemycins or derivatives thereof and surfactants, stabilizers and antioxidants.

The Examiner also contends that Chabala and Sutherland teach formulations comprising avermectins and milbemycins that utilize the same inactive ingredients as disclosed in the pending claims.

The Examiner also refers to Katoh, which pertains to the use of surfactants in a premix for an animal feed comprising macrolide compounds that are structurally analogous to avermectins.

Neither Beuvry, Chabala, Sutherland nor Katoh relate to the use of any stabilizers for decreasing or preventing decomposition of avermectins or milbemycins in anthelmintic formulations.

Carson, as stated by the Examiner, relates to the use of anhydrous citric acid in food stuffs to provide a pH range from about 3.0 to about 7.0 in order to minimize the breakdown of the components in the mixture. However, Carson relates to the use of buffers for stabilizing a *water suspension* of virginiamycin, and *not* a solid formulation.

The Examiner also alleges that Freehauf teaches the inclusion of avermectins and milbemycins in oral compositions wherein pH stabilizers such as maleic acid or citric acid are included. Freehauf relates to an oral veterinary paste consisting essentially of praziquantel and ivermectin. Freehauf mentions stabilizers such as citric acid/citrate to provide a pH range of 4 to 6.5. Since the main ingredient is praziquantel, it is not obvious that the same stabilizers will decrease or prevent decomposition of avermectins or milbemycins. Also, Freehauf relates to a paste formulation comprising polar solvents that will dissolve anthelmintic agents and macrolide anthelmintic compounds, while the present invention discloses solid materials as carrier vehicles.

In view of the foregoing arguments, it would not be obvious to one skilled in the art to propose the instantly claimed stabilized premix formulations comprising avermectins or milbemycins with an extended shelf life and methods of their preparation. Accordingly, none of the cited references teach or suggest methods for preventing acid/base catalyzed decomposition of avermectins and milbemycins.

For the foregoing reasons, none of the references cited by the Examiner, either alone or in combination, render the pending claims *prima facie* obvious. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.

**REQUEST FOR INTERVIEW**

If any issue remains as an impediment to allowance, an interview with the Examiner and SPE is respectfully requested, prior to issuance of any paper other than a Notice of Allowance; and, the Examiner is respectfully requested to contact the undersigned to arrange a mutually convenient time and manner for such an interview.




**CONCLUSION**

For the reasons stated above, Applicants respectfully request a favorable reconsideration of the application, reconsideration and withdrawal of the rejections of the pending claims, and prompt issuance of a Notice of Allowance.

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